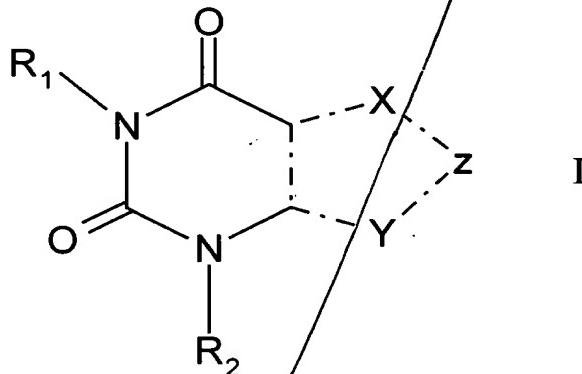


WHAT IS CLAIMED IS:

1. A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the following formula:



5

wherein:

X, Y and Z are independently selected from a member of the group consisting of C(R₃), N, N(R₃) and S;

R₁ is selected from a member of the group consisting of hydrogen, methyl, 10 C₍₅₋₉₎alkyl, C₍₅₋₉₎alkenyl, C₍₅₋₉₎alkynyl, C₍₅₋₉₎hydroxyalkyl, C₍₃₋₈₎alkoxyl, C₍₅₋₉₎alkoxyalkyl, the R₁ being optionally substituted;

R₂ and R₃ are independently selected from a member of the group consisting of hydrogen, halo, oxo, C₍₁₋₂₀₎alkyl, C₍₁₋₂₀₎hydroxyalkyl, C₍₁₋₂₀₎thioalkyl, C₍₁₋₂₀₎alkylamino, C₍₁₋₂₀₎alkylaminoalkyl, C₍₁₋₂₀₎aminoalkyl, C₍₁₋₂₀₎aminoalkoxyalkenyl, 15 C₍₁₋₂₀₎aminoalkoxyalkynyl, C₍₁₋₂₀₎diaminoalkyl, C₍₁₋₂₀₎triarninoalkyl, C₍₁₋₂₀₎tetraarninoalkyl, C₍₅₋₁₅₎aminotrialkoxyamino, C₍₁₋₂₀₎alkylamido, C₍₁₋₂₀₎alkylamidoalkyl, C₍₁₋₂₀₎amidoalkyl, C₍₁₋₂₀₎acetamidoalkyl, C₍₁₋₂₀₎alkenyl, C₍₁₋₂₀₎alkynyl, C₍₃₋₈₎alkoxyl, C₍₁₋₁₁₎alkoxyalkyl, and C₍₁₋₂₀₎dialkoxyalkyl;

with the proviso that R₁ is not an ω-1 secondary alcohol substituted C₍₅₋₈₎ alkyl
20 when both X and Y are N(R₃), Z is C(R₃) and R₃ is H or C₍₁₋₃₎ alkyl.

2. The therapeutic compound of claim 1, wherein R₁ is substituted with a member of the group consisting of N-OH, acylamino, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl (mercaptop), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and -NR^aR^b, wherein each of R^a and R^b may be the same or different and each is selected from the group consisting of hydrogen, optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl and heterocyclic group.

3. The therapeutic compound of claim 1, wherein R₂ and R₃ are selected from the group consisting of methyl, ethyl, oxo, isopropyl, n-propyl, isobutyl, n-butyl, t-butyl, 2-

hydroxyethyl, 3-hydroxypropyl, 3-hydroxy-n-butyl, 2methoxyethyl, 4-methoxy-n-butyl, 5-hydroxyhexyl, 2-bromopropyl, 3-dimethylaminobutyl, 4-chloropentyl, methylamino, aminomethyl, and methylphenyl.

4. The therapeutic compound of claim 1, wherein each R₂ and R₃ is substituted
5 with one or more members of the group consisting of hydroxyl, methyl, carboxyl, furyl,
furfuryl, biotinyl, phenyl, naphthyl, amino group, amido group, carbamoyl group, cyano
group, sulfo, sulfonyl, sulfinyl, sulfhydryl, sulfeno, sulfanilyl, sulfamyl, sulfamino,
phosphino, phosphinyl, phospho, phosphono, N-OH, -Si(CH₃)₃, C₍₁₋₃₎alkyl,
C₍₁₋₃₎hydroxyalkyl, C₍₁₋₃₎thioalkyl, C₍₁₋₃₎alkylamino, benzyldihydrocinnamoyl group,
10 benzoyldihydrocinnamido group, optionally substituted heterocyclic group and optionally
substituted carbocyclic group.

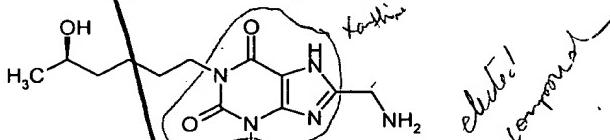
5. The therapeutic compound of claim 4, wherein the heterocyclic group or
carbocyclic group is substituted with one or more members of the group consisting of
halo, hydroxyl, nitro, SO₂NH₂, C₍₁₋₆₎alkyl, C₍₁₋₆₎haloalkyl, C₍₁₋₈₎alkoxyl, C₍₁₋₁₁₎alkoxyalkyl,
15 C₍₁₋₆₎alkylamino, and C₍₁₋₆₎aminoalkyl.

6. The therapeutic compound of claim 4, wherein the heterocyclic group is a
member selected from the group consisting of acridinyl, aziridinyl, azocinyl, azepinyl,
benzimidazolyl, benzodioxolanyl, benzofuranyl, benzothiophenyl, carbazole, 4a H-
carbazole, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, dioxoindolyl,
20 furazanyl, furyl, furfuryl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl,
indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindolinyl,
isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthalenyl, naphthyridinyl,
norbornanyl, norpinanyl, octahydroisoquinolinyl, oxazolidinyl, oxazolyl, oxiranyl,
perimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl,
25 phenoxythiinyl, phenoxyazinyl, phenyl, phthalazinyl, piperazinyl, piperidinyl, 4-piperidonyl,
piperidyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl,
pyrenyl, pyridazinyl, pyridinyl, pyridyl, pyridyl, pyrimidinyl, pyrrolidinyl, 2-pyrrolidonyl,
pyrrolonyl, pyrrolyl, 2H-pyrrolyl, quinazolinyl, 4H-quinolizinyl, quinolinyl, quinoxalinyl,
30 quinuclidinyl, β-carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl,
tetrazolyl, 6H-1,2,5-thiadiazinyl, 2H-,6H-1,5,2-dithiazinyl, thianthrenyl, thiazolyl, thienyl,
thiophenyl, triazinyl, xanthenyl and xanthinyl.

7. The therapeutic compound of claim 4, wherein the carbocyclic group is a
member selected from the group consisting of adamantyl, anthracenyl, benzamidyl,
benzyl, bicyclo[2.2.1]heptanyl, bicyclo[2.2.1]hexanyl, bicyclo[2.2.2]octanyl,
35 bicyclo[3.2.0]heptanyl, bicyclo[4.3.0]nonanyl, bicyclo[4.4.0]decanyl, biphenyl,
biscyclooctyl, cyclobutyl, cyclobutenyl, cycloheptyl, cycloheptenyl, cyclohexanedionyl,
cyclohexenyl, cyclohexyl, cyclooctanyl, cyclopentadienyl, cyclopentanedionyl,

cyclopentenyl, cyclopentyl, cyclopropyl, decalinyl, 1,2-diphenylethanyl, indanyl, 1-indanonyl, indenyl, naphthyl, naphthalenyl, phenyl, resorcinolyl, stilbenyl, tetrahydronaphthyl, tetralinyl, tetralonyl, and tricyclododecanyl.

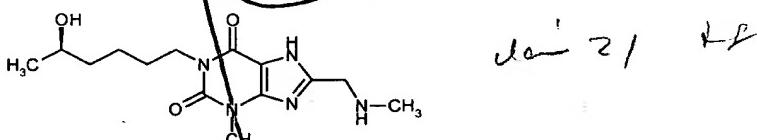
8. A compound having the formula



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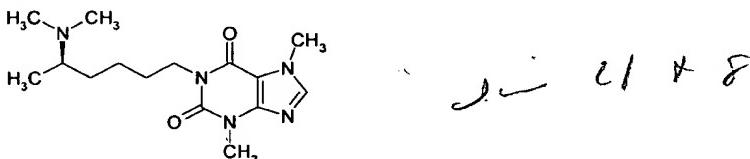
or a pharmaceutically acceptable salt thereof.

9. A compound having the formula



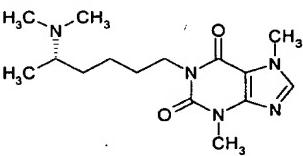
10 or a pharmaceutically acceptable salt thereof.

10. A compound having the formula



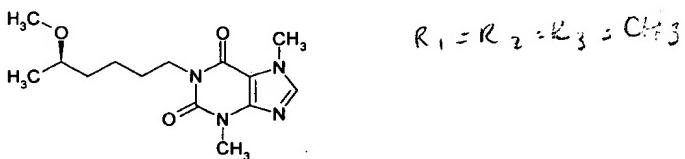
or a pharmaceutically acceptable salt thereof.

11. A compound having the formula



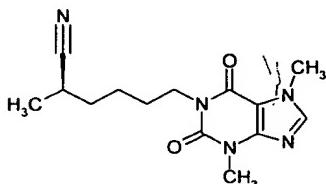
15

12. A compound having the formula



or a pharmaceutically acceptable salt thereof.

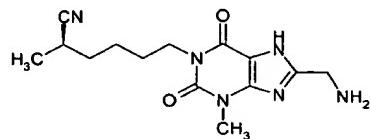
13. A compound having the formula



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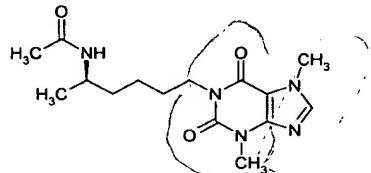
or a pharmaceutically acceptable salt thereof.

14. A compound having the formula



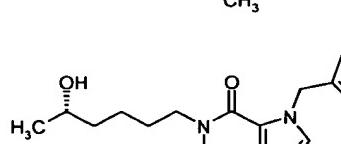
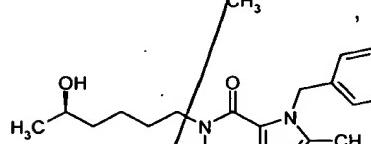
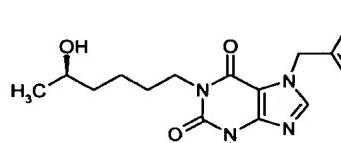
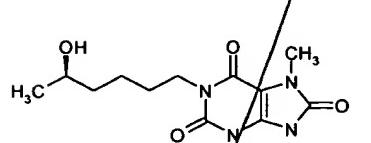
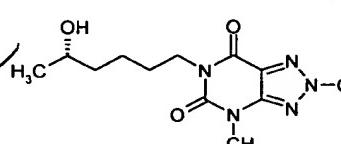
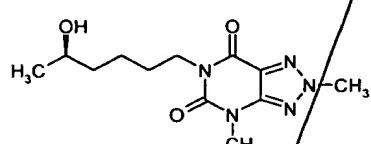
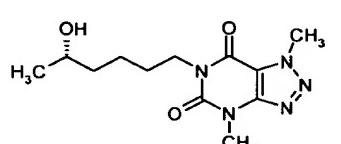
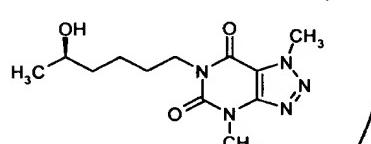
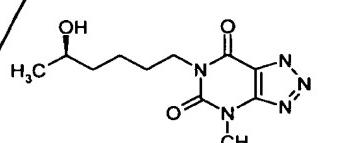
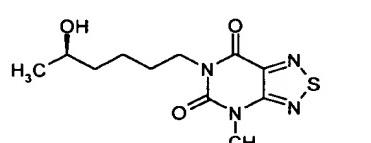
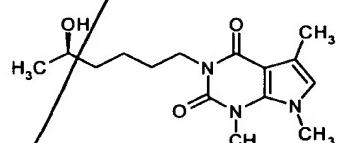
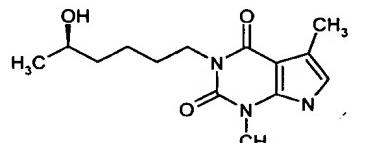
or a pharmaceutically acceptable salt thereof.

5 15. A compound having the formula



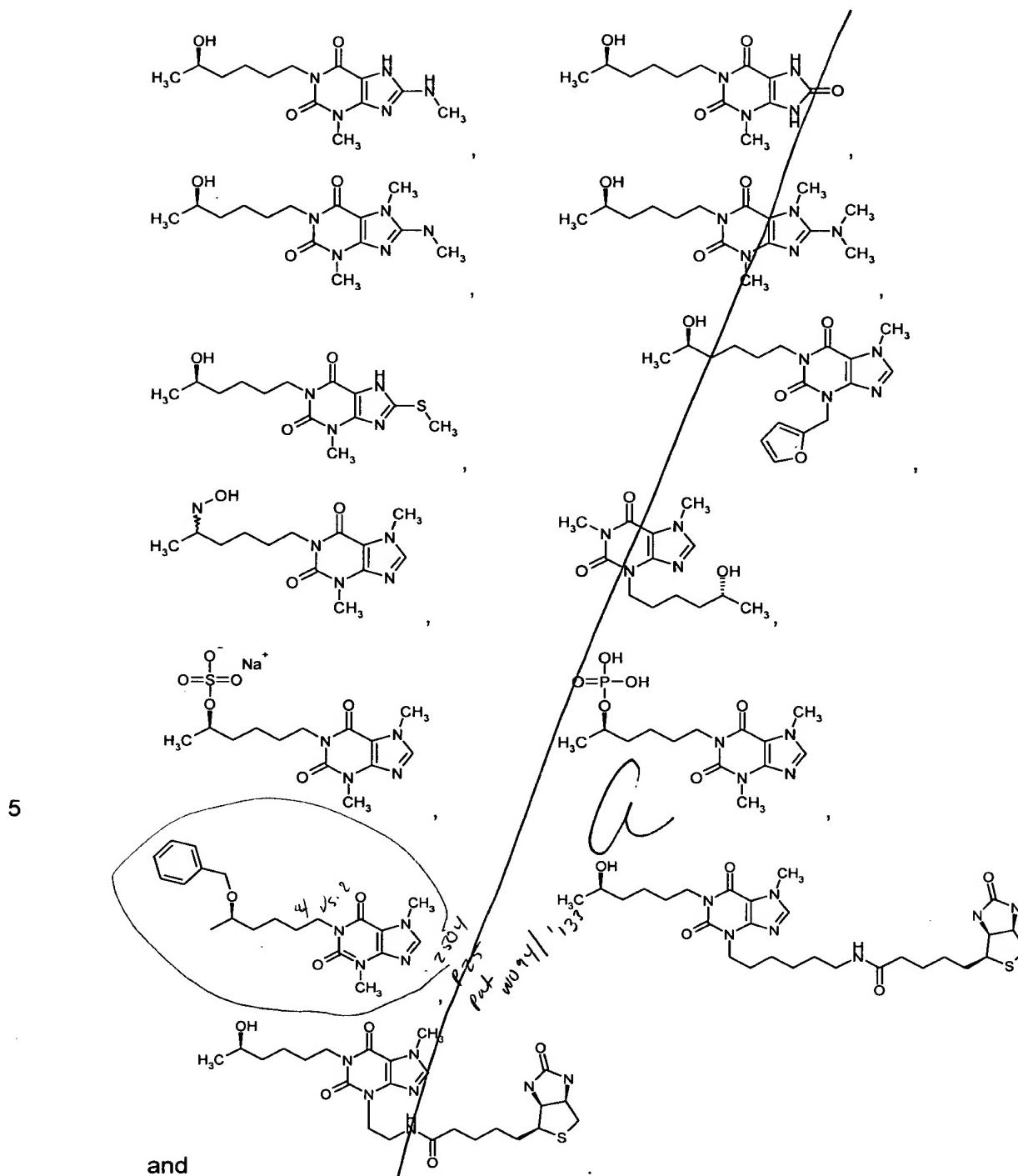
or a pharmaceutically acceptable salt thereof.

16. A compound, or pharmaceutically acceptable salt thereof, selected from the group consisting of:



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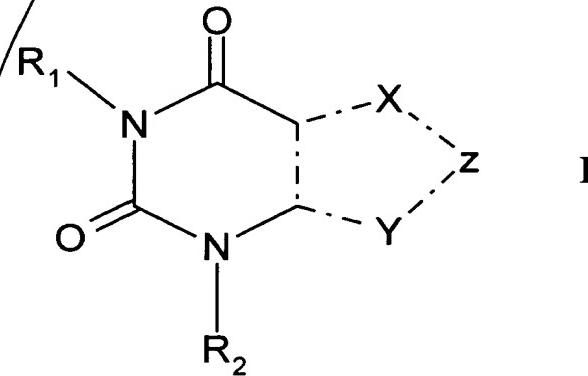
10 18. A pharmaceutical composition comprising the compound of either claim 1, 8 or 9-17 in admixture with a pharmaceutically acceptable carrier, adjuvant or vehicle.

19. A method for inhibiting a cellular process or activity mediated by IL-12, the method comprising:

15 (a) contacting IL-12 responsive cells with a compound as defined in claim 1, 8 or 9-17; and

- (b) determining that the cellular process or activity mediated by IL-12 is inhibited.
20. The method of claim 19, wherein step (a) is carried out *in vitro*.
21. The method of claim 19, wherein said cellular process is the differentiation of naïve T cells into Th1 cells.
- 5 22. The method of claim 19, wherein said activity is the secretion of proinflammatory cytokines.
23. The method of claim 22, wherein said cytokines are secreted by Th1 cells.
24. A method for treating a Th1 cell-mediated inflammatory response in a mammal in need of such treatment, the method comprising:
- 10 administering to the mammal a therapeutically effective amount of the compound defined in either claim 1, 8 or 9-17, wherein said compound is capable of inhibiting an IL-12 mediated cellular process or activity, thereby inhibiting the inflammatory response.
- 15 25. The method of claim 24, wherein the inflammatory response is associated with a disease or condition selected from the group consisting of chronic inflammatory disease, chronic intestinal inflammation, arthritis, psoriasis, asthma and autoimmune disorders.
26. The method of claim 25, wherein the inflammatory response is associated with an autoimmune disorder.
- 20 27. The method of claim 26, wherein said autoimmune disorder is selected from type-1 IDDM, multiple sclerosis, rheumatoid arthritis, uveitis, inflammatory bowel disease, lupus disorders, and acute and chronic graft-versus-host disease.
28. The method of claim 24, wherein said mammal is a human.
29. A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the following formula:

25



wherein:

X, Y and Z are independently selected from a member of the group consisting of C(R₃), N, N(R₂) and S;

R₁ is selected from a member of the group consisting of hydrogen, methyl, substituted alkyl, C₍₅₋₉₎alkenyl, C₍₅₋₉₎alkynyl, C₍₅₋₉₎hydroxyalkyl, C₍₃₋₈₎alkoxyl, C₍₅₋₉₎alkoxyalkyl, the R₁ being optionally substituted;

- R₂ and R₃ are independently selected from a member of the group consisting of
- 5 hydrogen, halo, oxo, C₍₁₋₂₀₎alkyl, C₍₁₋₂₀₎hydroxyalkyl, C₍₁₋₂₀₎thioalkyl, C₍₁₋₂₀₎alkylamino, C₍₁₋₂₀₎alkylaminoalkyl, C₍₁₋₂₀₎aminoalkyl, C₍₁₋₂₀₎aminoalkoxyalkenyl, C₍₁₋₂₀₎aminoalkoxyalkynyl, C₍₁₋₂₀₎diaminoalkyl, C₍₁₋₂₀₎triarninoalkyl, C₍₁₋₂₀₎tetraarninoalkyl, C₍₅₋₁₅₎aminotrialkoxyamino, C₍₁₋₂₀₎alkylamido, C₍₁₋₂₀₎alkylamidoalkyl, C₍₁₋₂₀₎amidoalkyl, C₍₁₋₂₀₎acetamidoalkyl, C₍₁₋₂₀₎alkenyl, C₍₁₋₂₀₎alkynyl, C₍₃₋₈₎alkoxyl, C₍₁₋₁₁₎alkoxyalkyl, and 10 C₍₁₋₂₀₎dialkoxyalkyl;

with the proviso that R₁ is not an ω-1 secondary alcohol substituted C₍₅₋₈₎ alkyl when both X and Y are N(R₃), Z is C(R₃) and R₃ is H or C₍₁₋₃₎ alkyl.

30. The therapeutic compound of claim 29, wherein R₁ is substituted with a member of the group consisting of N-OH, acylamino, cyano group, sulfo, sulfonyl, 15 sulfinyl, sulfhydryl (mercaptopo), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and -NR^aR^b, wherein each of R^a and R^b may be the same or different and each is selected from the group consisting of hydrogen, optionally substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl and heterocyclic group.

- 20 31. The therapeutic compound of claim 29, wherein R₂ and R₃ are selected from the group consisting of methyl, ethyl, oxo, isopropyl, n-propyl, isobutyl, n-butyl, t-butyl, 2-hydroxyethyl, 3-hydroxypropyl, β-hydroxy-n-butyl, 2methoxyethyl, 4-methoxy-n-butyl, 5-hydroxyhexyl, 2-bromopropyl, 3-dimethylaminobutyl, 4-chloropentyl, methylamino, aminomethyl, and methylphenyl.

- 25 32. The therapeutic compound of claim 29, wherein each R₂ and R₃ is substituted with one or more members of the group consisting of hydroxyl, methyl, carboxyl, furyl, furfuryl, biotinyl, phenyl, naphthyl, amino group, amido group, carbamoyl group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl, sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono, N-OH, -Si(CH₃)₃, C₍₁₋₃₎alkyl, 30 C₍₁₋₃₎hydroxyalkyl, C₍₁₋₃₎thioalkyl, C₍₁₋₃₎alkylamino, benzylidihydrocinnamoyl group, benzoyldihydrocinnamido group, optionally substituted heterocyclic group and optionally substituted carbocyclic group.

- 35 33. The therapeutic compound of claim 32, wherein the heterocyclic group or carbocyclic group is substituted with one or more members of the group consisting of halo, hydroxyl, nitro, SO₂NH₂, C₍₁₋₆₎alkyl, C₍₁₋₆₎haloalkyl, C₍₁₋₈₎alkoxyl, C₍₁₋₁₁₎alkoxyalkyl, C₍₁₋₆₎alkylamino, and C₍₁₋₆₎aminoalkyl.

34. The therapeutic compound of claim 32, wherein the heterocyclic group is a member selected from the group consisting of acridinyl, aziridinyl, azocinyl, azepinyl, benzimidazolyl, benzodioxolanyl, benzofuranyl, benzothiophenyl, carbazole, 4a H-carbazole, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, dioxoindolyl, furazanyl, furyl, furfuryl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthalenyl, naphthyridinyl, norbornanyl, norpinanyl, octahydroisoquinolinyl, oxazolidinyl, oxazolyl, oxiranyl, perimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxythiinyl, phenoxyazinyl, phenyl, phthalazinyl, piperazinyl, piperidinyl, 4-piperidonyl, piperidyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyrenyl, pyridazinyl, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolonyl, pyrrolyl, 2H-pyrrolyl, quinazolinyl, 4H-quinolizinyl, quinolinyl, quinoxalinyl, quinuclidinyl, β -carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 2H-,6H-1,5,2-dithiazinyl, thianthrenyl, thiazolyl, thienyl, thiophenyl, triazinyl, xanthenyl and xanthinyl.

35. The therapeutic compound of claim 32, wherein the carbocyclic group is a member selected from the group consisting of adamantyl, anthracenyl, benzamidyl, benzyl, bicyclo[2.2.1]heptanyl, bicyclo[2.2.1]hexanyl, bicyclo[2.2.2]octanyl, bicyclo[3.2.0]heptanyl, bicyclo[4.3.0]nonanyl, bicyclo[4.4.0]decanyl, biphenyl, biscyclooctyl, cyclobutyl, cyclobutetyl, cycloheptyl, cycloheptenyl, cyclohexanedionyl, cyclohexenyl, cyclohexyl, cyclooctanyl, cyclopentadienyl, cyclopentanedionyl, cyclopentenyl, cyclopentyl, cyclopropyl, decalinyl, 1,2-diphenylethanyl, indanyl, 1-indanonyl, indenyl, naphthyl, naphthalenyl, phenyl, resorcinolyl, stilbenyl, tetrahydronaphthyl, tetralinyl, tetralonyl, and tricyclododecanyl.

36. A pharmaceutical composition comprising the compound of claim 29 in admixture with a pharmaceutically acceptable carrier, adjuvant or vehicle.

37. A method for inhibiting a cellular process or activity mediated by IL-12, the method comprising:

30 (a) contacting IL-12 responsive cells with a compound as defined in claim 29; and

(b) determining that the cellular process or activity mediated by IL-12 is inhibited.

38. The method of claim 37, wherein step (a) is carried out *in vitro*.

39. The method of claim 37, wherein said cellular process is the differentiation of 35 naⁱve T cells into Th1 cells.

40. The method of claim 37, wherein said activity is the secretion of proinflammatory cytokines.

41. The method of claim 40, wherein said cytokines are secreted by Th1 cells.
42. A method for treating a Th1 cell-mediated inflammatory response in a mammal in need of such treatment, the method comprising:
 - 5 administering to the mammal a therapeutically effective amount of the compound defined in claim 29, wherein said compound is capable of inhibiting an IL-12 mediated cellular process or activity, thereby inhibiting the inflammatory response.
43. The method of claim 42, wherein the inflammatory response is associated with a disease or condition selected from the group consisting of chronic inflammatory disease, chronic intestinal inflammation, arthritis, psoriasis, asthma and autoimmune disorders.
- 10 44. The method of claim 43, wherein the inflammatory response is associated with an autoimmune disorder.
45. The method of claim 44, wherein said autoimmune disorder is selected from type-1 IDDM, multiple sclerosis, rheumatoid arthritis, uveitis, inflammatory bowel disease, lupus disorders, and acute and chronic graft-versus-host disease.
- 15 46. The method of claim 42, wherein said mammal is a human.

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Add A27